

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: West, *et al.*

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Examiner: Bowers, Nathan A.

For: **MICROFLUIDIC INTEGRATED MICROARRAYS FOR
BIOLOGICAL DETECTION**DATE OF ELECTRONIC DEPOSIT: October 26, 2009

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Sir:

APPELLANTS' REPLY BRIEF PURSUANT TO 37 C.F.R. § 41.41

As Appellants explained in their opening brief, the Examiner did not establish a *prima facie* case of obviousness because the obviousness rejections are based on a combination of prior art references that teach away from combination with one another and also away from the claimed invention. Even if the Examiner had established a *prima facie* case of obviousness – which Appellants do not concede – Appellants submitted evidence showing that the claimed invention performs 96 times faster than the cited prior art cited by the Examiner, which objective evidence rebuts such a *prima facie* case of obviousness.

Insisting that a *prima facie* case of obviousness may be based on improperly combined references, the Examiner in his Answer¹ now attempts to sidestep the aforementioned teaching away. But the Examiner's arguments are based on an incomplete review of the references, and the Examiner cannot cure the references' inability to support a *prima facie* case of obviousness.

The Examiner also attacks Appellants' objective evidence of superior performance. But this attack is without merit because it is based on an incorrect legal standard and because

¹ Appellants observe that page 1 of the Examiner's Answer refers to "Application Number 11/000,309," filed November 30, 2004, by Yoneda *et al.*, but that the body of the Answer refers to the present application.

the Examiner fails to consider all of Appellants' evidence. Because the Examiner's Answer provides no legal or factual support for the rejections, the rejections should be withdrawn and the claims should be allowed. *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992) ("If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is **entitled to grant of the patent**") (emphasis added).

I. ARGUMENT

The Examiner's Answer attempts to sidestep the facts that (1) the cited references teach away from combination with one another and away from the claimed invention; and (2) Appellants' invention represents a 96-fold improvement in performance over the cited prior art. The Examiner's positions are contrary to governing law and to the facts of record, and cannot rescue his improper obviousness rejections.

A. The Examiner Cannot Justify Combining References That Teach Away From Their Combination And Away From The Claimed Invention

As set forth in Appellants' opening brief, the Examiner's proposed Mathies-McNeely-Quake combination cannot support a *prima facie* case of obviousness because (1) the references teach away from combination with one another; and (2) the references teach away from the claimed invention (Appellants' Opening Brief ("Opening Br.") at 6-9). In his Answer, the Examiner attempts to evade this teaching away by recharacterizing the content of the McNeely reference. But a full review of the reference reveals that the Examiner's recharacterization is based on a misleading partial quotation of the McNeely reference and that the McNeely reference cannot support the obviousness rejections.

Appellants' microfluidic chips include, *inter alia*, channels having a depth of less than about 10 microns. As Appellants explained in their opening brief, the McNeely reference relied upon by the Examiner requires that fluidic channels have a height of **at least 15 microns**, which teaches away from the Quake reference (channels must be **2-5 microns** in height) *and* away from the claimed invention (channels are less than **10 microns** in height).

In his Answer, the Examiner suggests that McNeely does not teach away from channels less than 15 microns in height, and intimates that McNeely's "at least about 15 micron" height requirement can be disregarded:

“McNeely expresses an interest in even smaller microarray channels/chambers in paragraph [0084] (**‘while it is desirable to have a small reaction chamber volume . . .’**), but cannot obtain smaller sizes due to his reliance on providing a gasket between the base substrate and coverslip” (Answer at 26) (emphasis added)

The Examiner’s argument is, however, based on an incomplete quotation of McNeely. (Absent evidence to the contrary, Appellants will presume this was an unintentional oversight on the part of the Examiner.) McNeely paragraph [0084] in fact states:

“The height of [the] reaction chamber 11 is defined by the thickness of [the] gasket . . . In the preferred embodiment of the invention, [the gasket] has a thickness of at least about 15 μ m.[.] As gasket thickness is decreased, roughness of the slide surface and lower surface of the interface device, and nonuniformity of the gasket may become problematic. Moreover, if the gasket thickness is decreased further, the chamber may become too difficult to fill. Therefore, while it is desirable to have a small reaction chamber volume, it appears that reducing the volume by reducing the chamber height causes problems if the height goes below about a certain height” (McNeely at [0084]) (emphasis added).

The properly quoted language emphasized above highlights that reducing the chamber height results in the chamber **“becoming too difficult to fill”** and that **“reducing the chamber height causes problems if the height goes below about a certain height”** (McNeely at [0084]) (emphasis added). That reduced chamber height makes the chamber “difficult to fill” and “causes problems” is a clear teaching away from chambers having a height of less than the 15 microns, and the Examiner never confronts this critical aspect of McNeely paragraph [0084]. See *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1550 (Fed. Cir. 1983) (reversing finding of obviousness where district court erred by “considering the references in less than their entireties”). The Examiner’s Answer thus fails to escape the references’ teaching away, and the Examiner accordingly cannot establish a *prima facie* case of obviousness. See *Ecolochem, Inc. v. Southern Cal. Edison Co.*, 227 F.3d 1361, 1373-75 (Fed. Cir. 2000) (reversing district court’s finding of obviousness where cited references taught away from their combination); *In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983) (references that teach away from their combination do not support obviousness rejection). Without a *prima facie* case of obviousness, Appellants’ claims are allowable, and the Board need go no further. See *In re Oetiker*, 977 F.2d at 1445 (“If examination at the initial stage

does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent”) (emphasis added).

B. The Examiner’s Analysis Of Appellants’ Objective Evidence Of Superior Performances Is Mistaken As A Matter Of Fact And As A Matter Of Law

Even if the Examiner had made out a *prima facie* case of obviousness, which Appellants do not concede, the strength (or lack thereof) of such a case is irrelevant to the ultimate obviousness conclusion: “[i]f rebuttal evidence of adequate weight is produced, the holding of *prima facie* obviousness, being but a legal inference from previously uncontradicted evidence, is dissipated. Regardless of whether the *prima facie* case could have been characterized as strong or weak, the examiner must consider all of the evidence anew.” *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir. 1984). Thus, patentability “is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.” *In re Oetiker*, 977 F.2d at 1445. Under this standard, an applicant need only provide evidence to support patentability that is, by only the smallest degree, more convincing than an examiner’s evidence to the contrary. *Id.*

In the present case, Appellants presented evidence that the claimed invention represents a **96-fold** improvement over the Examiner’s cited prior art (Opening Br. at 9-10). *See In re Wiechert*, 370 F.2d 927, 962 (C.C.P.A. 1967) (Rich, J.) (**7-fold** improvement of activity over the prior art sufficient to rebut *prima facie* case of obviousness); *see also Takeda Chem. Indus. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1355 (Fed. Cir. 2007) (superior performance relative to prior art rebutted *prima facie* case of obviousness). The Examiner now seeks to downplay that evidence, but because the Examiner’s arguments misapply controlling law, mischaracterize the cited prior art, and fail to challenge Appellants’ evidence, his position is without merit.

1. The Examiner misapplies the law governing the submission of objective evidence

The Examiner first claims that Appellants’ evidence is deficient because “it fails to compare the results of the invention of the instant application with results obtained by the systems of Mathies and McNeely” (Answer at 28). But that is not the law. Instead, an applicant meets their burden by comparing the claimed invention with the closest prior art. *In re Merchant*, 575 F.2d 865, 869 (C.C.P.A. 1978); *In re Geiger*, 815 F.2d 686, 689 (Fed. Cir. 1987) (Newman, J., concurring). Here, Appellants demonstrated that the claimed invention achieves hybridization in 5 minutes, which represents a 96-fold improvement over the very

prior art the Examiner has cited, thus satisfying their burden. *Id.*; see also Opening Br. at 9-10. The Examiner's attempt to avoid the demonstrated superiority of the claimed invention over the cited prior art ignores controlling law and is without merit.

2. The Examiner's characterization of the prior art is contrary to controlling Federal Circuit law

The Examiner also seeks to minimize Appellants' demonstrated superiority over the prior art by attempting to recharacterize the content of the prior art. But the Examiner's position is based on impermissible speculation that is contrary to controlling law regarding the proper interpretation of prior art references.

More specifically, the McNeely reference (against which Appellants demonstrate their 96-fold superiority) states that hybridization processes according to that invention are "typically performed **overnight**" (McNeely at [0153], emphasis added). The Examiner's attempt to avoid this aspect of the reference in his Answer bears repeating in full:

"The fact that McNeely leaves the microarray out 'overnight' in no way means that the microarray hybridization reaction actually requires 8 hours to be completed. It **could be** completed within an hour, and just sit there for the rest of the night. It **could be** completed in less time" (Answer at 28-29) (emphasis added).

But "**could be**" is not the correct legal standard. Instead, as the Federal Circuit has made clear, "[o]bviousness cannot be predicated on what is unknown." *In re Rijckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993). Hence, "[t]he mere fact that a certain thing **may result** from a given set of circumstances **is not sufficient**." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added). McNeely plainly states that devices according to that invention perform hybridization "overnight," and the Examiner's unsupported speculation to the contrary conflicts with controlling law. *In re Rijckaert*, 9 F.3d at 1534.²

3. The Examiner's arguments ignore Appellants' evidence of record

The Examiner finally suggests that Appellants' evidence of superior performance should be discounted because the height of the channels in Appellants' provided journal article is 15 microns, which is the same height as the microchannel height set forth in

² The Examiner points to no evidence of record to support his disregarding of the term "overnight" in McNeely, thus underscoring that his argument lacks basis in the record. *In re Zurko*, 258 F.3d 1379, 1386 (Fed. Cir. 2001) ("the [Examiner] cannot simply reach conclusions based on [his] own understanding or experience . . . Rather, the [Examiner] must point to some concrete evidence in the record in support of these findings").

McNeely (Answer at 29). The Examiner then goes on: “[i]t is not understood how Appellant obtains unexpected results if the microarray is structurally the same as that set forth by McNeely” (Answer at 29).

The Examiner’s argument ignores Appellants’ evidence. See *In re Alton*, 76 F.3d 1168, 1176 (Fed. Cir. 1996) (error not to consider all evidence supplied by applicant to overcome rejection). In the present case, Appellants’ March 25, 2008 declaration and Exhibit B attached thereto illustrate that devices according to the claimed invention achieve hybridization in about 5 minutes, which is 96 times faster than the McNeely reference (Opening Br. at 9-10, 25 ¶¶ 6-7, 36-37). Accordingly, Appellants’ evidence of superior performance is commensurate with the scope of the claims, and the Examiner’s Answer does not address this aspect of Appellants’ evidence. Accordingly, absent any argument to the contrary, Appellants have met their burden, and the claims are patentable. *In re Oetiker*, 977 F.2d at 1445 (“patentability is determined on the totality of the record, by a **preponderance of evidence with due consideration to persuasiveness of argument**”) (emphasis added).

The Examiner’s attack on the journal article attached to Appellants’ declaration as Exhibit C thereto is also misplaced (Answer at 29). Appellants do not dispute that the article attached to Appellants’ March 25, 2008 declaration discloses channels that are 15 microns in height and that McNeely likewise discloses channels that are 15 microns in height. Based on this single commonality, the Examiner asserts that the devices described in the journal article are “structurally the same” as devices disclosed by McNeely and that the results in the journal article are “due to structural features present in the tested device of the declaration, but not present as limitations in the claimed invention of the instant application” (Answer at 29).

This argument misses the point. It is black-letter law that a claimed invention must be considered on the evidence as a whole, and Appellants have shown (Opening Br. at 9-10, 25 ¶¶ 6-7, 36-37) that devices according to the claimed invention is demonstrably superior to the Examiner’s cited prior art. But the Examiner does not provide any argument against *that* aspect of Appellants’ evidence. Instead, the Examiner identifies a commonality between the journal article – evidence that the Examiner characterizes as disclosing devices having channel sizes *outside the scope of the claims* – and the prior art. But by ignoring the evidence showing that devices made according to the claimed invention achieve hybridization in about 5 minutes (Opening Br. at 9-10, 25 ¶¶ 6-7, 36-37), the Examiner fails to consider the evidence “as a whole,” and fails to provide any substantive argument against Appellants’ evidence. Absent any substantive argument by the Examiner to oppose Appellants’ evidence,

Appellants' claims are patentable. *In re Oetiker*, 977 F.2d at 1445 ("patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument"). Accordingly, the Examiner provides no reason to discount Appellants' objective evidence of a 96-fold improvement over the prior art, which evidence is sufficient to overcome a *prima facie* case of obviousness. *See In re Wiechert*, 370 F.2d at 962 (7-fold improvement of activity over the prior art sufficient to rebut *prima facie* obviousness).

C. Separate Argument for Dependent Claims

The patentability of the pending dependent claims will stand or fall together with claim 1, as explained at pages 11-12 of Appellants' opening brief.

II. CONCLUSION

Applying incorrect legal standards and ignoring the facts of record, the Examiner's Answer attempts to manufacture a *prima facie* case of obviousness by improperly combining references and seeks to undercut Appellants' objective evidence of superior results. But application of the correct legal standards and a complete review of the prior art in the case makes clear that the cited prior art references expressly teach away from combination with one another *and* away from the claimed invention, and thus cannot support a *prima facie* case of obviousness. Because the Examiner does not establish a *prima facie* case of obviousness, the claims should be passed to allowance for this reason alone. *See In re Oetiker*, 977 F.2d at 1445 ("If examination at the initial stage does not produce a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent.")

Given that the Examiner fails to make out a *prima facie* case, it is unnecessary for the Board to go any further. In any event, even if the Examiner's reference combination were proper, Appellants' objective evidence shows that the performance of the claimed invention is superior to the prior art by two orders of magnitude, which evidence the Examiner counters with nothing more than speculation regarding the content of the prior art. *See id.* ("patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument"). Accordingly, because the Examiner fails to make out a *prima facie* case of obviousness and never meaningfully challenges the evidence of superior performance, the rejections should be vacated and Appellants' claims should be passed to allowance.

Respectfully submitted,

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